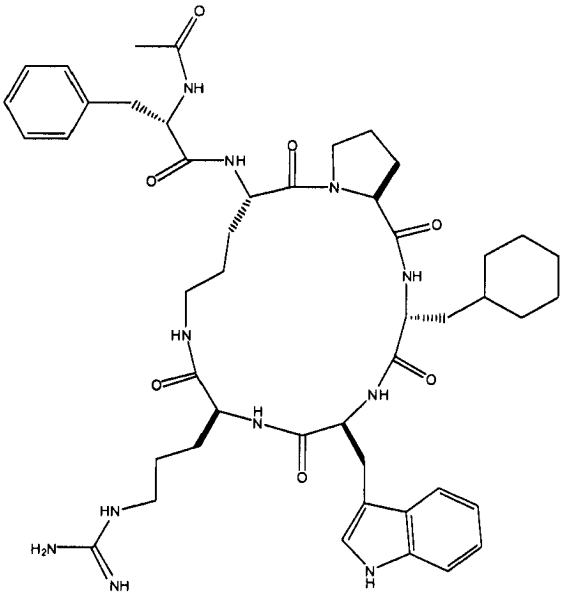
1. AMENDMENTS TO THE SPECIFICATION:

Please replace the paragraph appearing in the substitute specification filed on 4/14/05 at page 5 lines 12-17, with the following amended paragraph, which supersedes the intervening amendments filed on 6/29/06 and 10/16/07:

The compound is preferably an antagonist of C5a receptors on human and mammalian cells including, but not limited to, human polymorphonuclear leukocytes and human macrophages. The compound preferably binds potently and selectively to C5a receptors, and more preferably has potent antagonist activity at sub-micromolar concentrations. Even more preferably the compound has a receptor affinity ~~IC50<25μM~~ $IC_{50} < 25$ μM, and an antagonist potency ~~IC50 |μ~~ $IC_{50} < 1$ μM.

Please replace the paragraph appearing in the substitute specification filed on 4/14/05 at page 5 lines 18-22, with the following amended paragraph, which supersedes the intervening amendments filed on 6/29/06 and 10/16/07:

Most preferably the compound is selected from the group consisting of compounds **1** to **6, 10** to **15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33** to **37, 39** to **45, 47** to **50, 52** to **58 and 60** to **70** described in ~~provisional application~~PCT International Patent Application No. PCT/AU02/01427 (which gave rise to United States Patent Appl. Serial No. 10/493,117, published 9/28/06 as 20060217530), including the following compounds:



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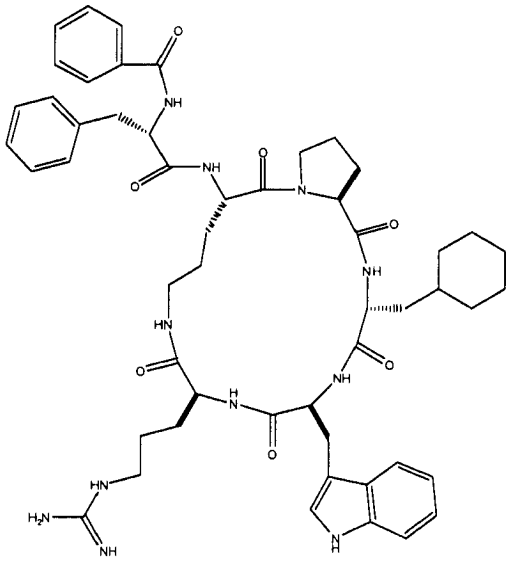

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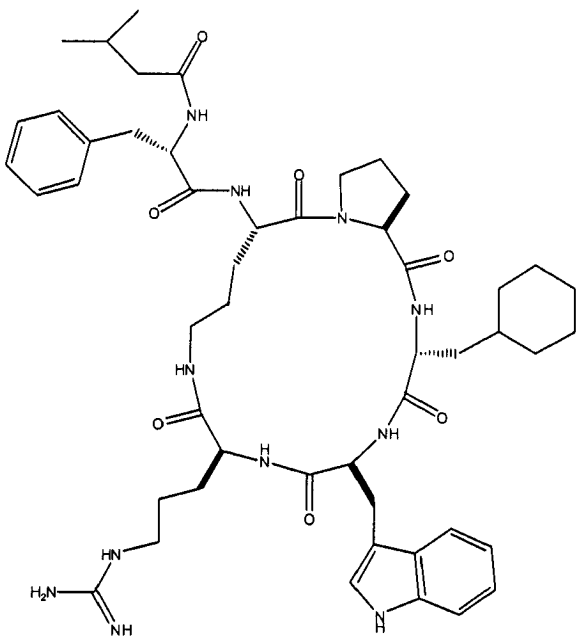

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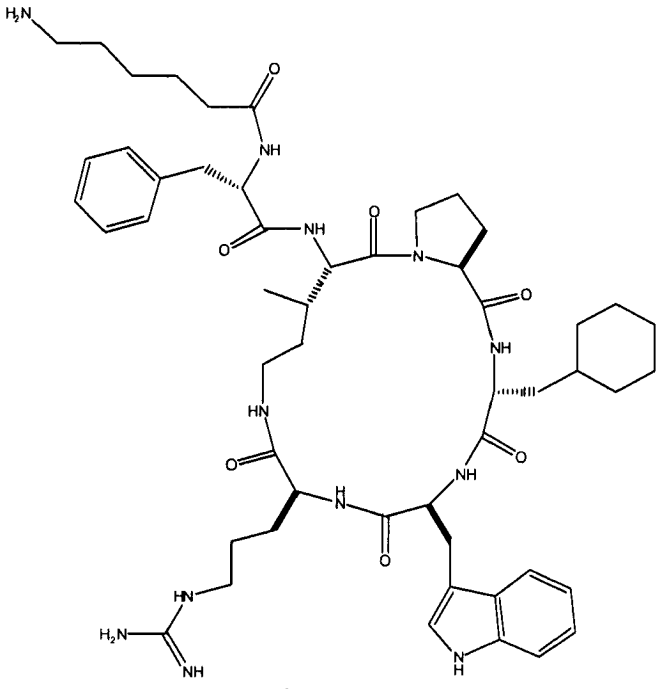

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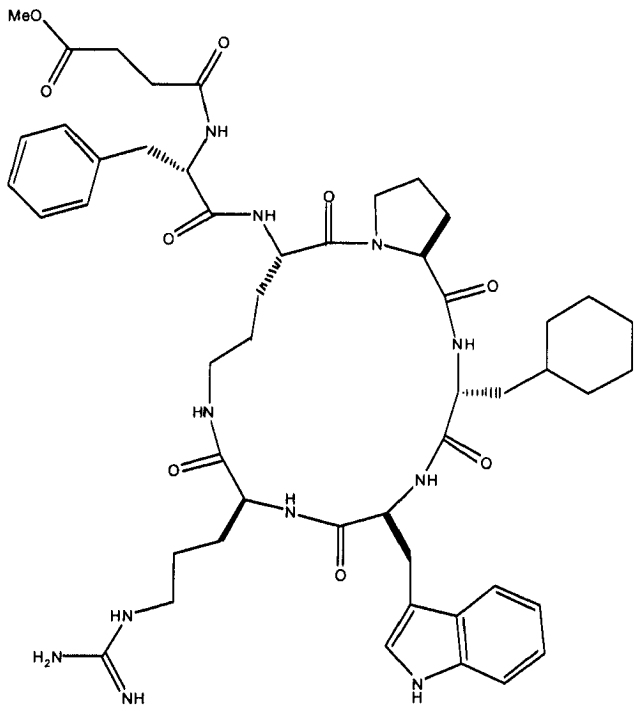
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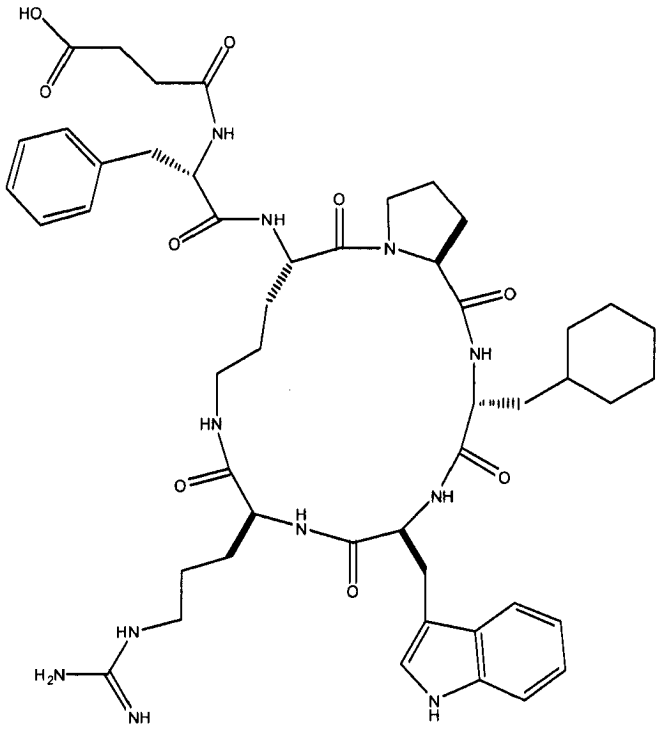
5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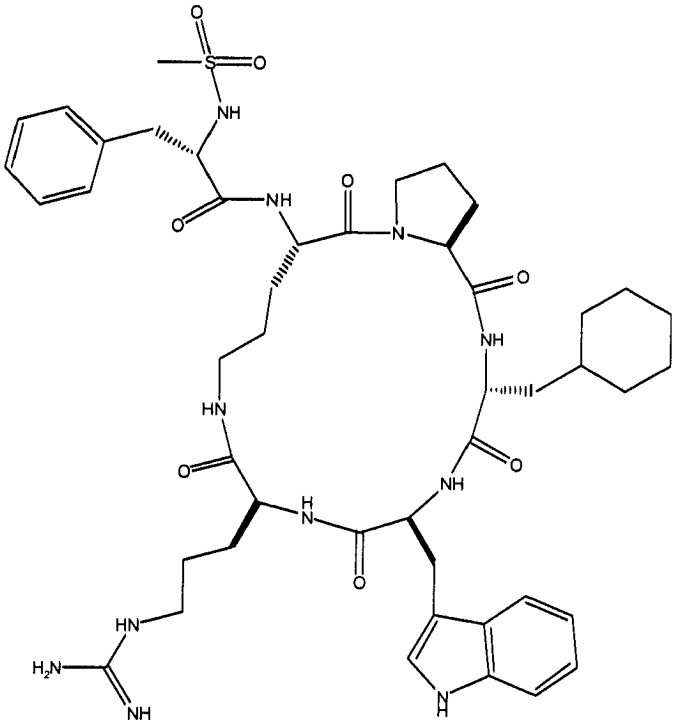

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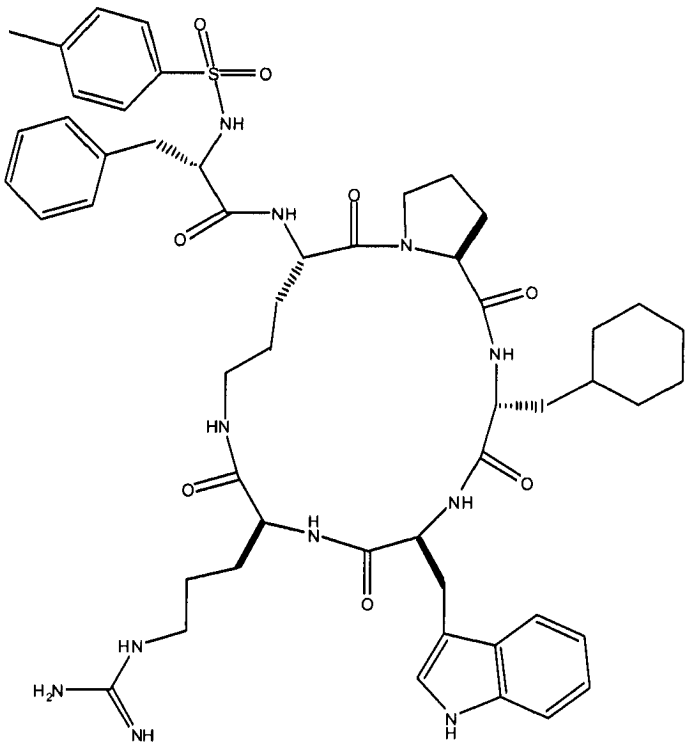

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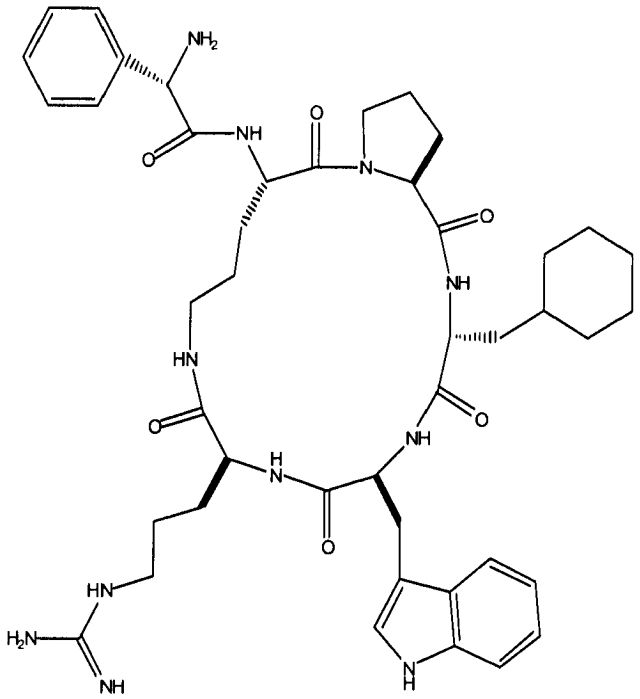

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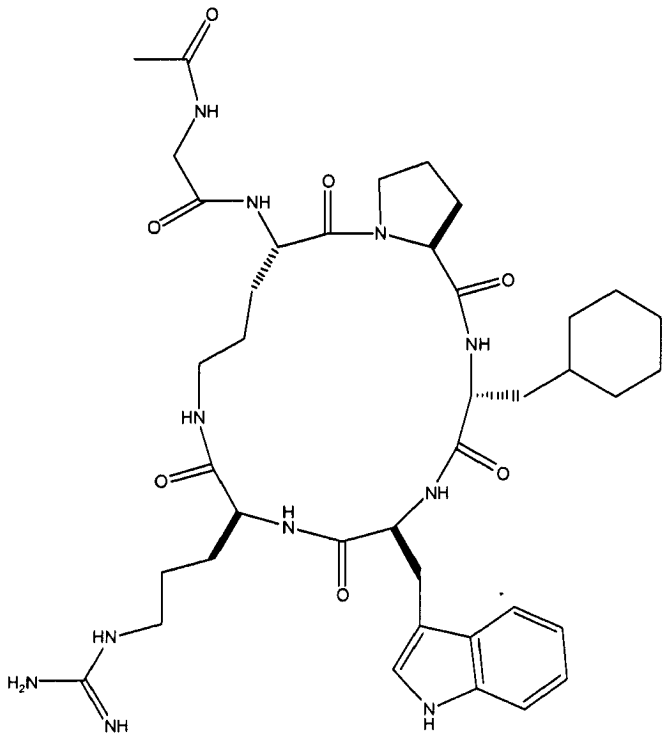

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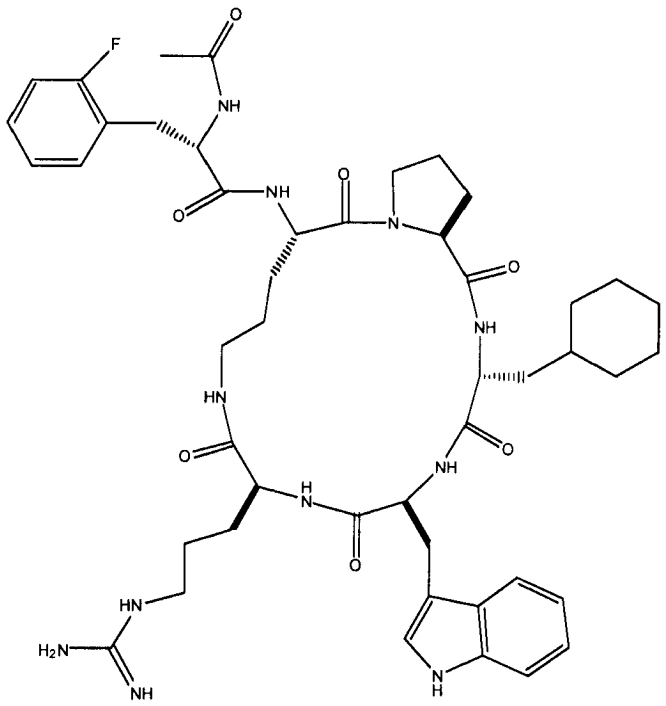

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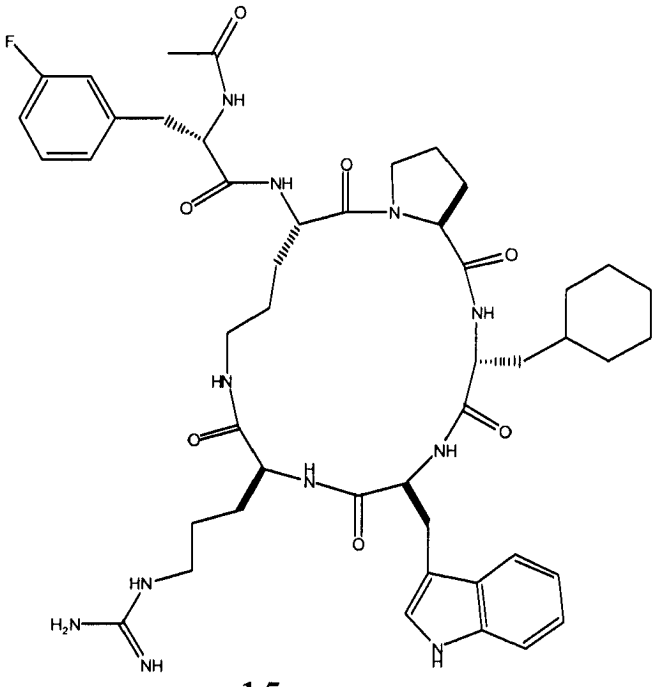

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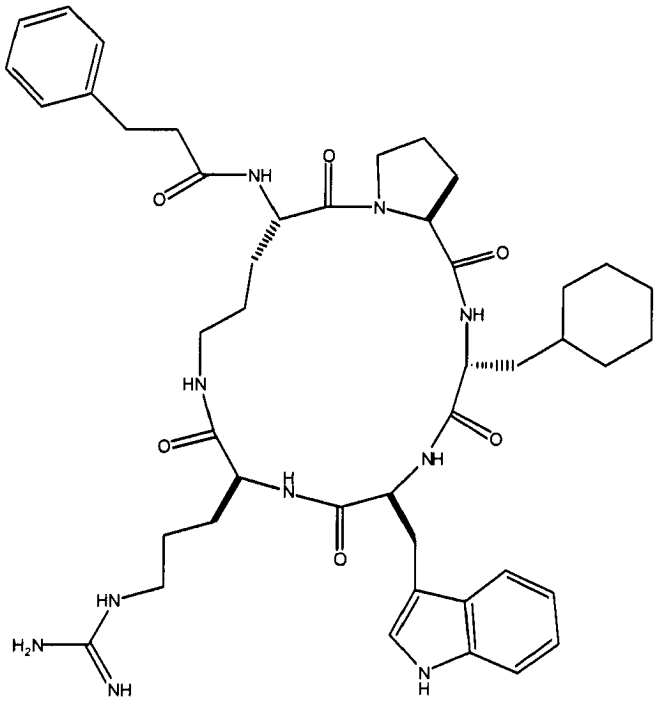

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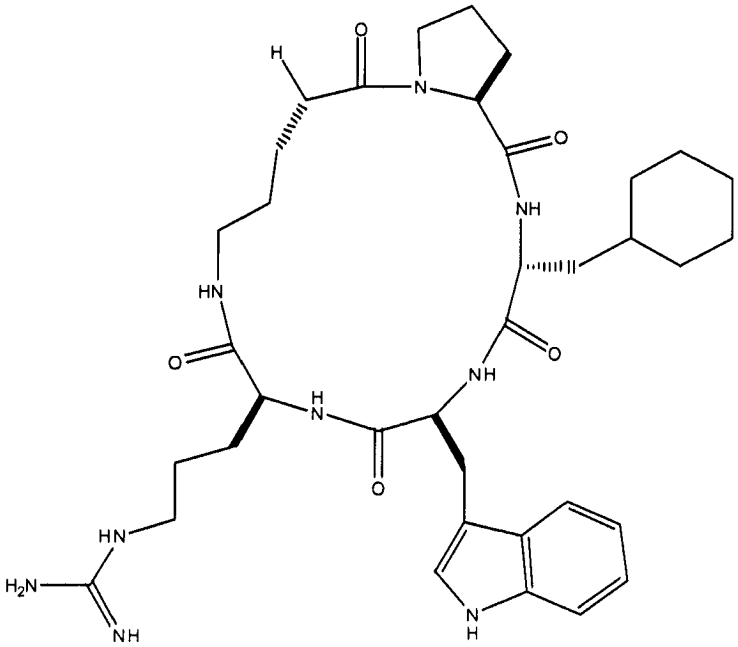

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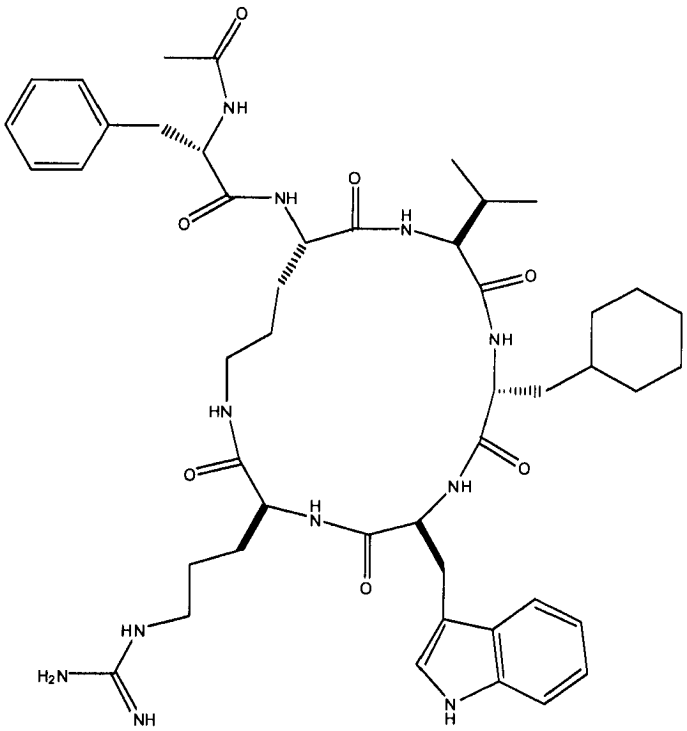

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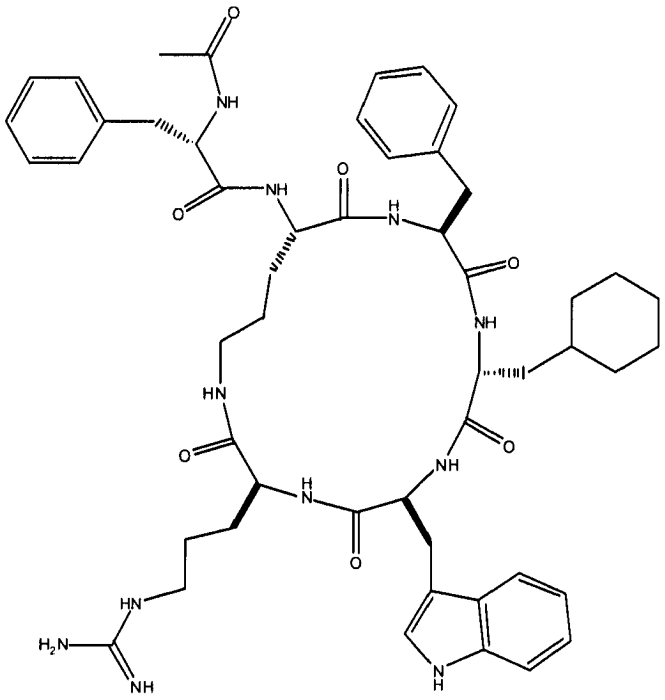

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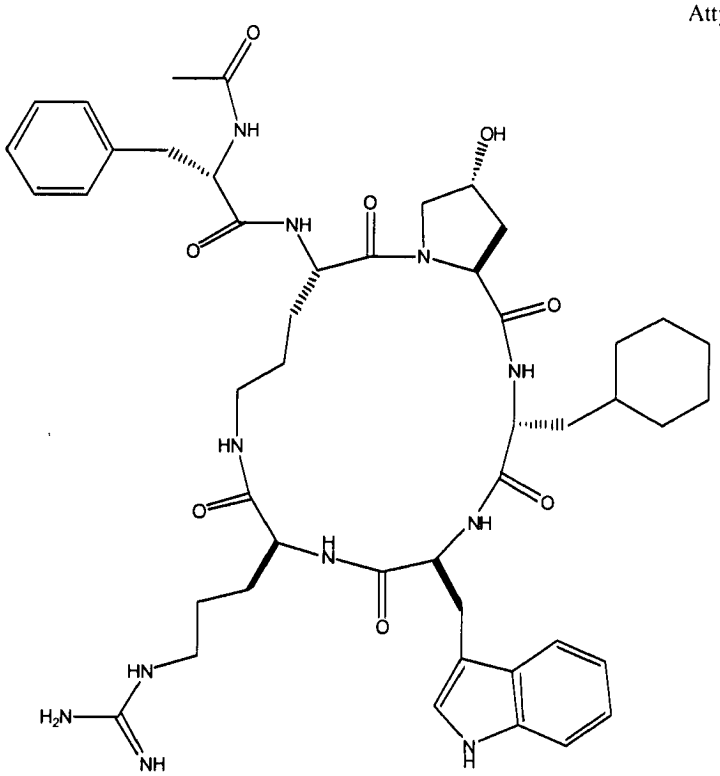

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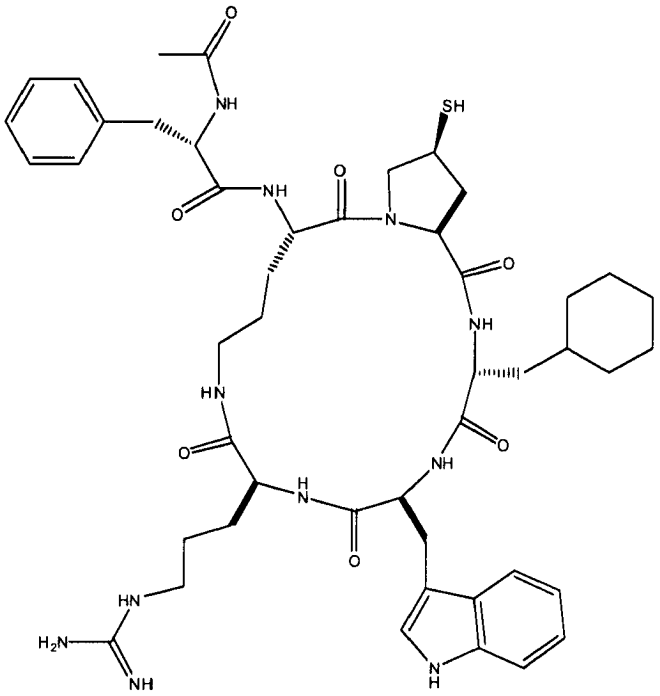

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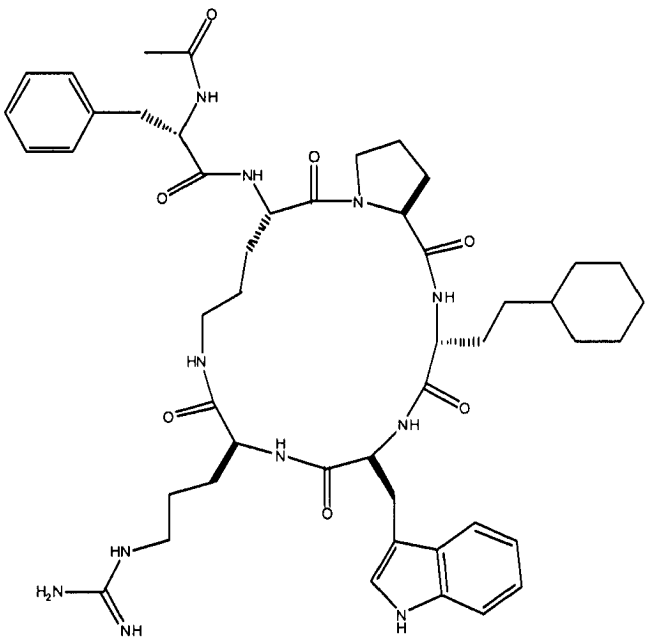

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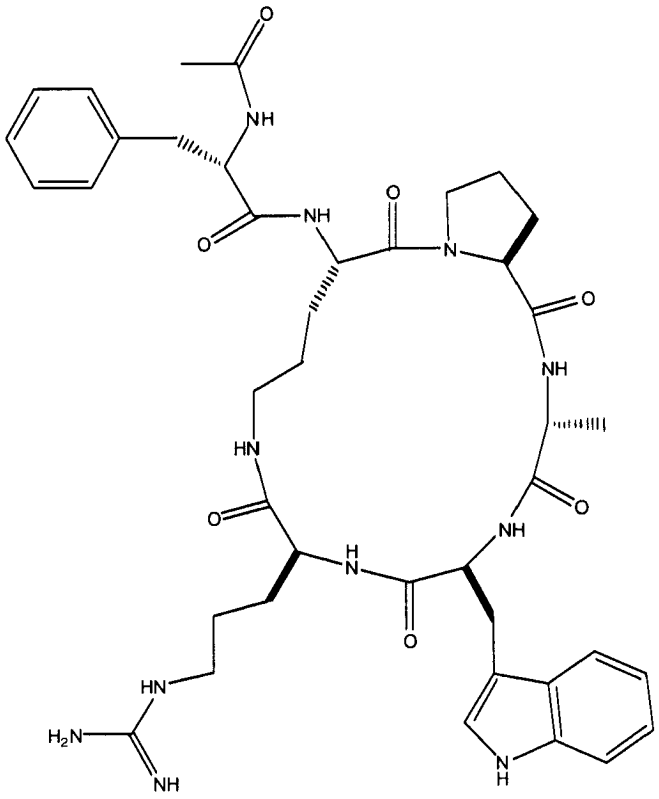

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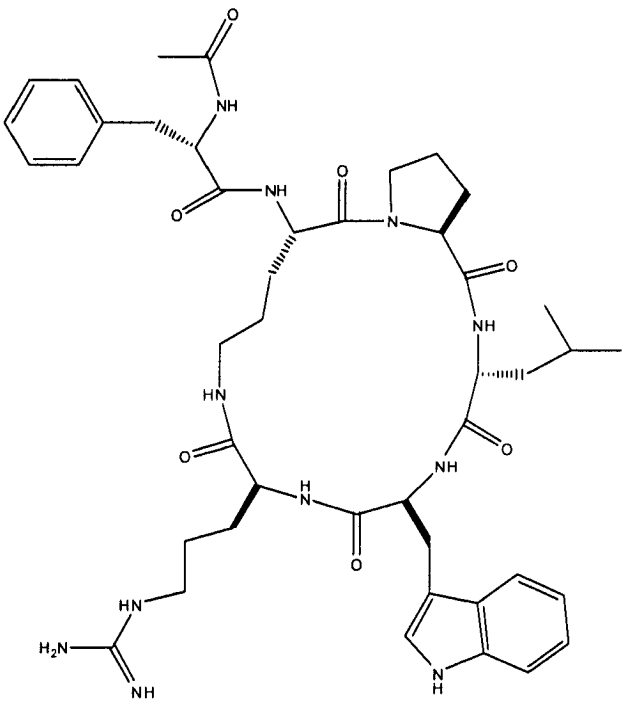

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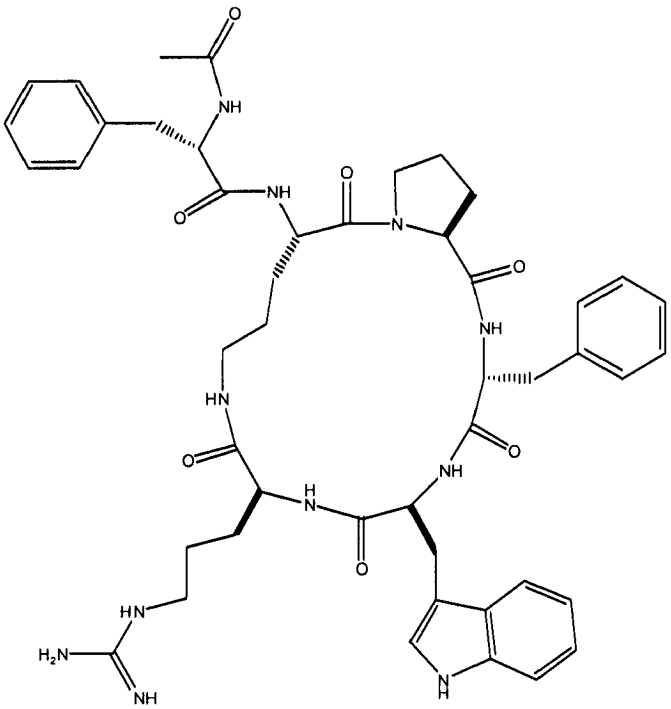

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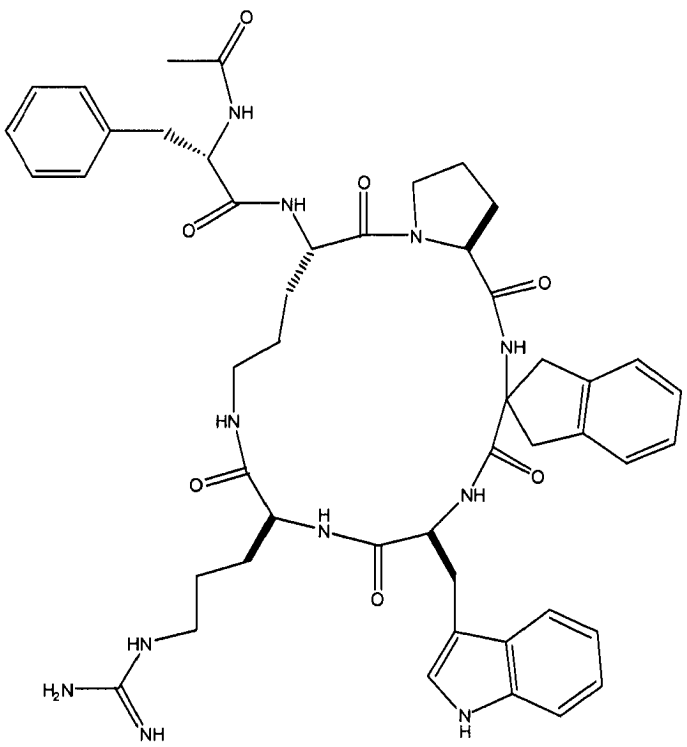

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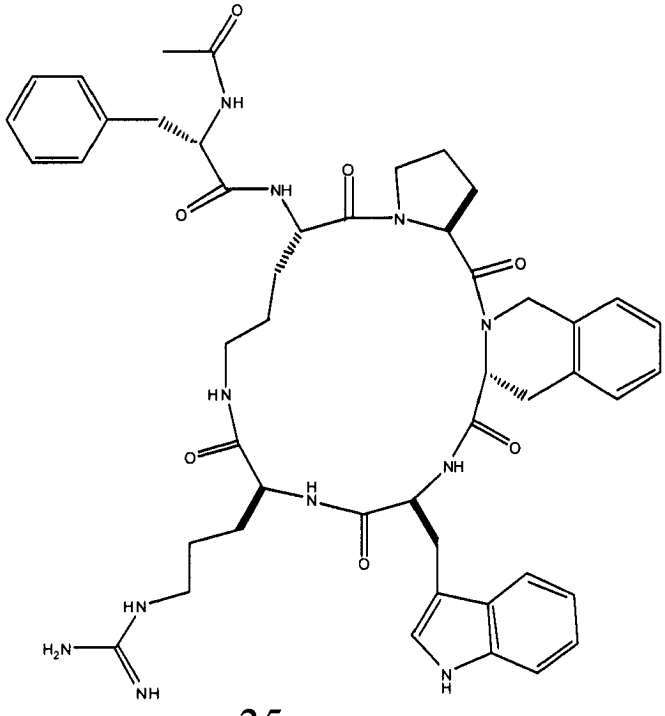

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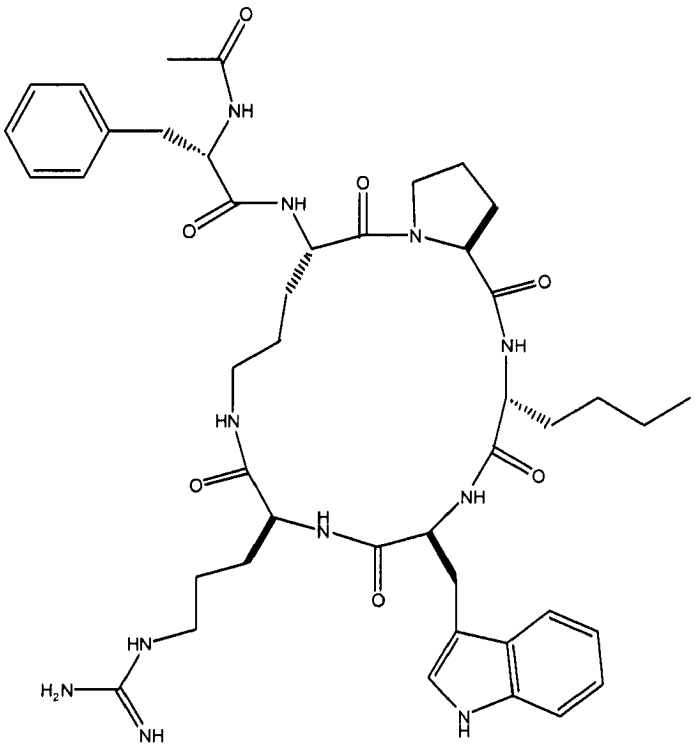

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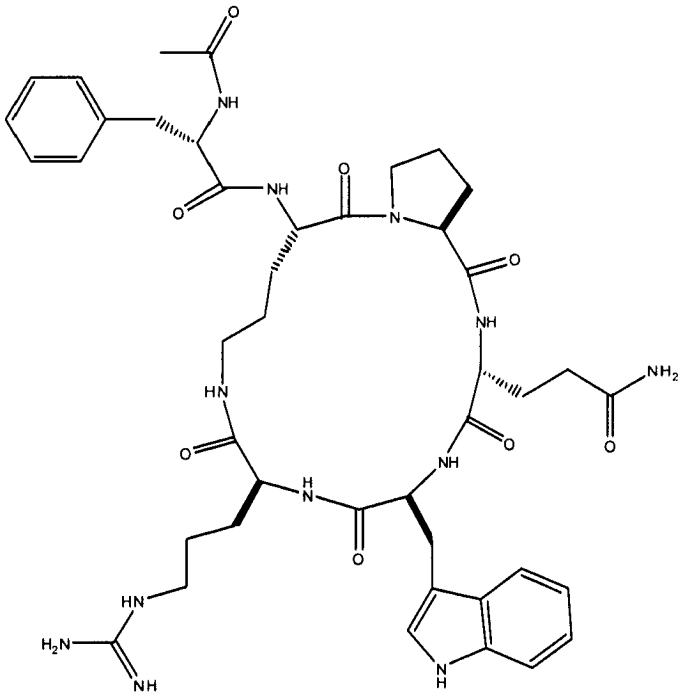

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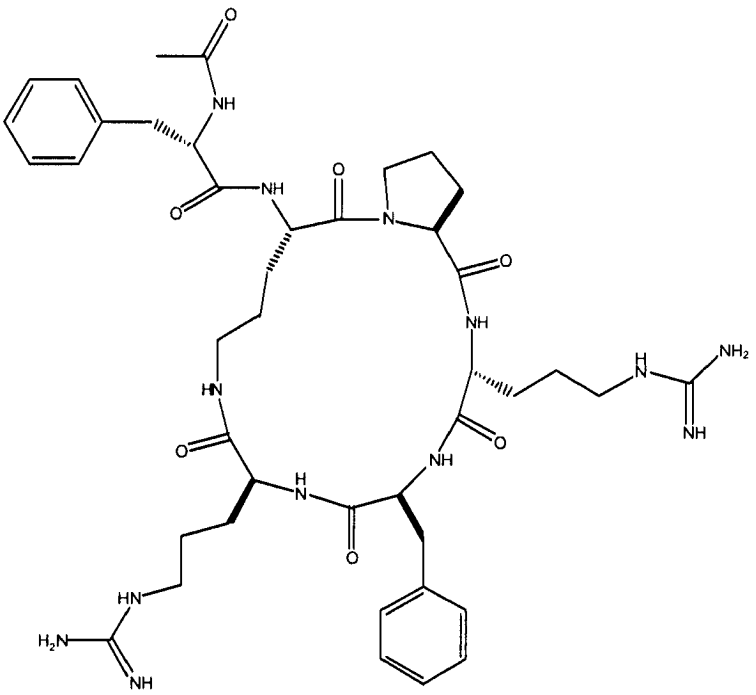

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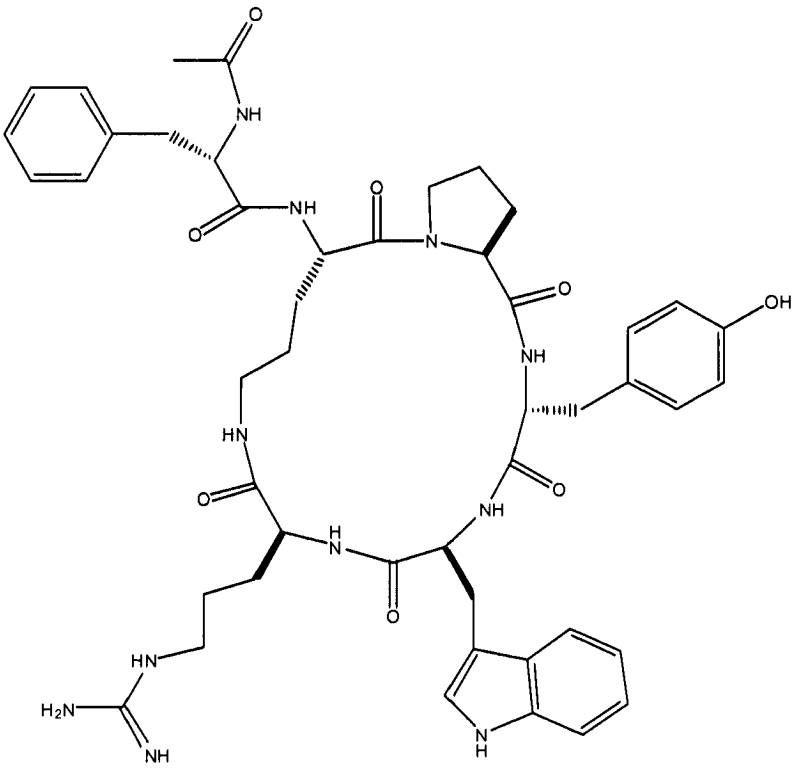

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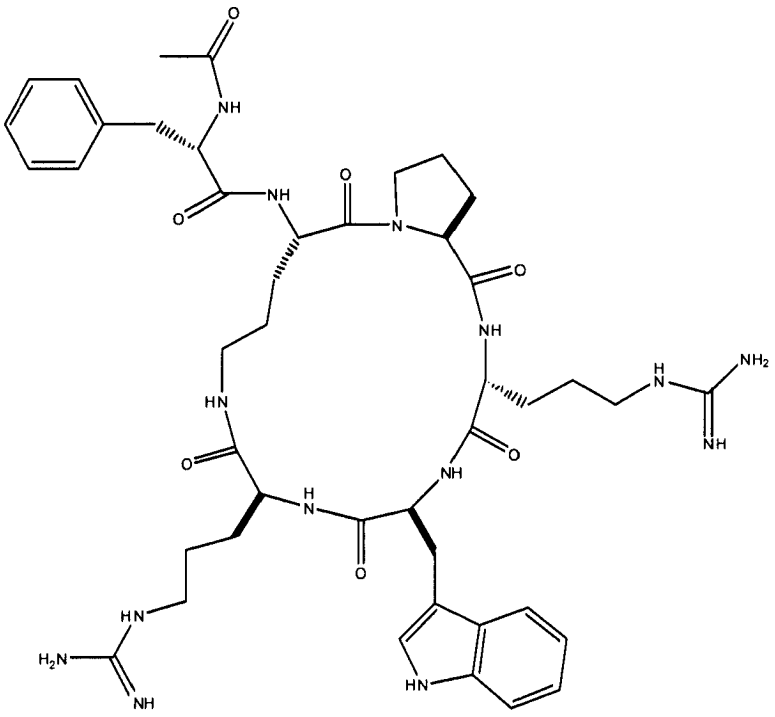

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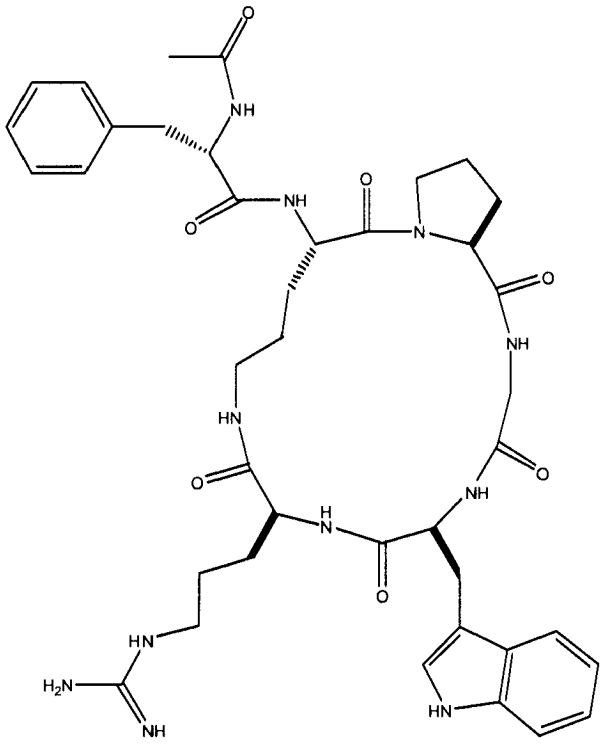

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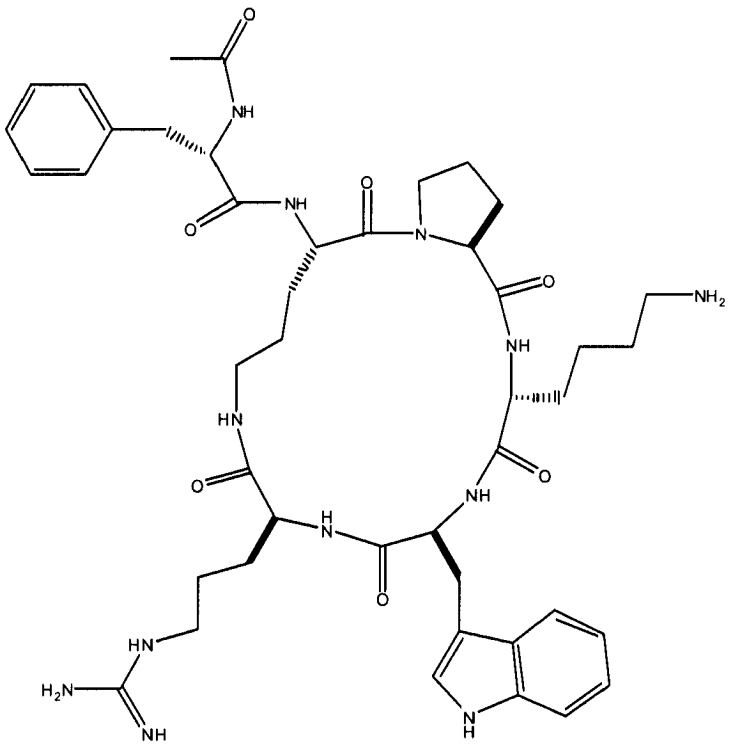

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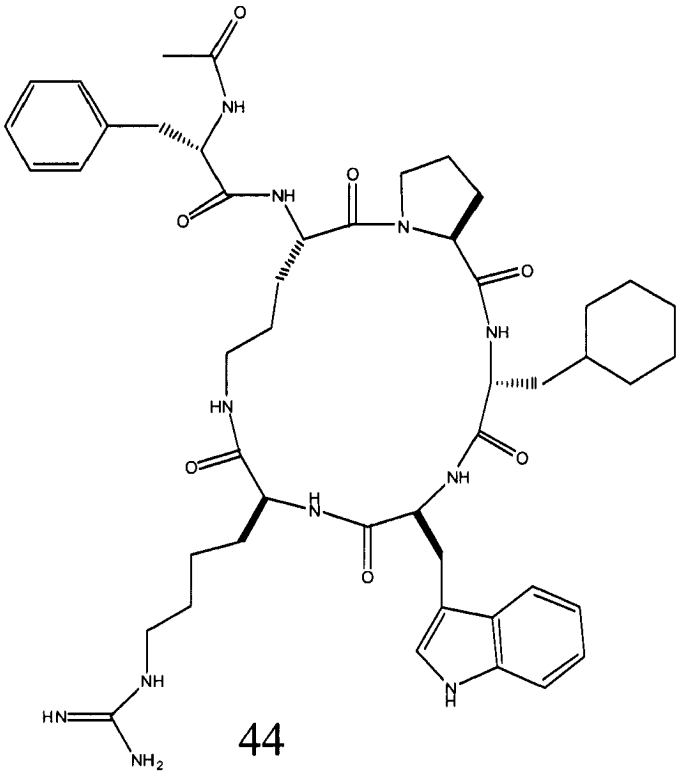

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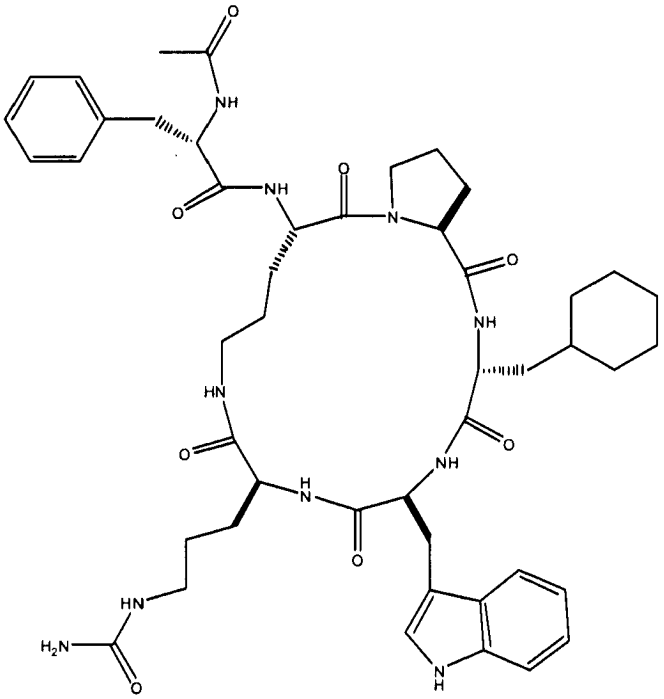

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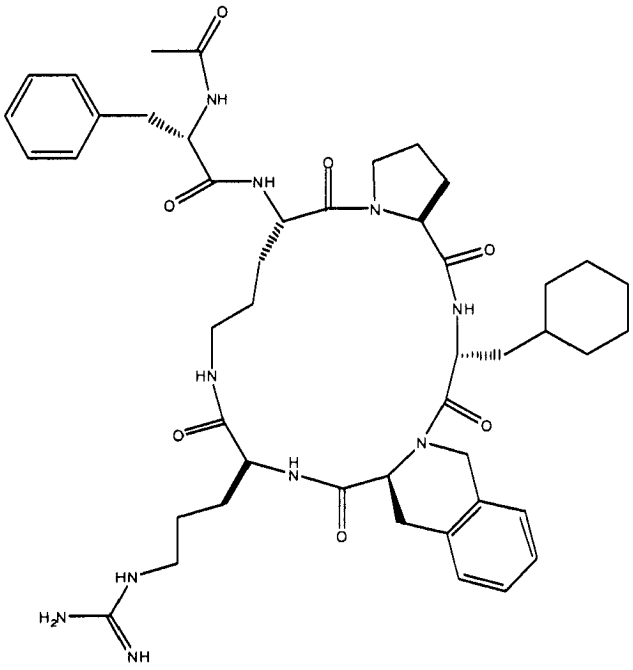

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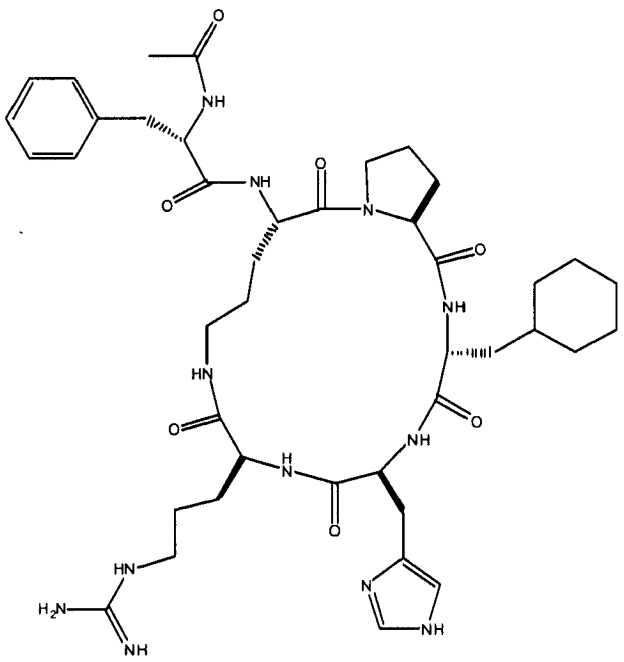

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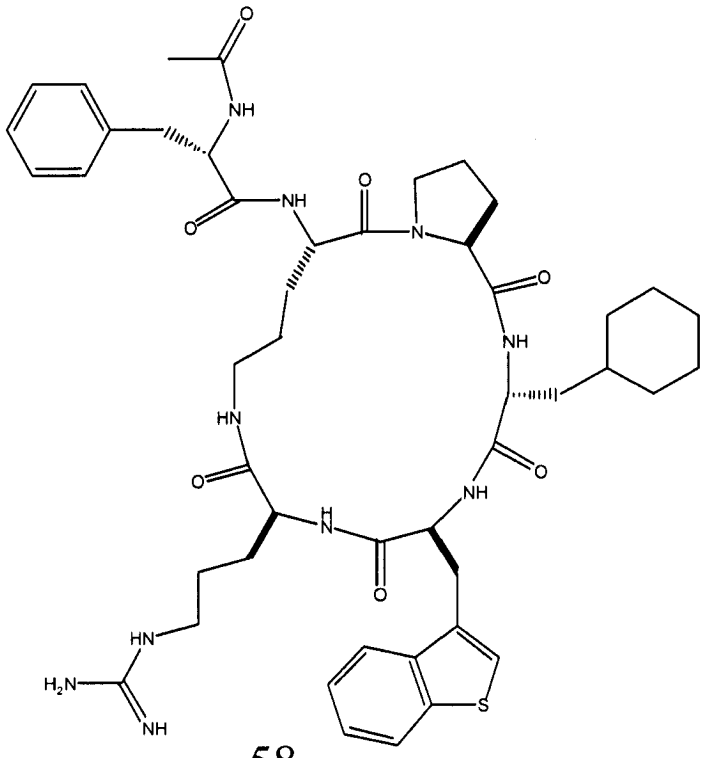

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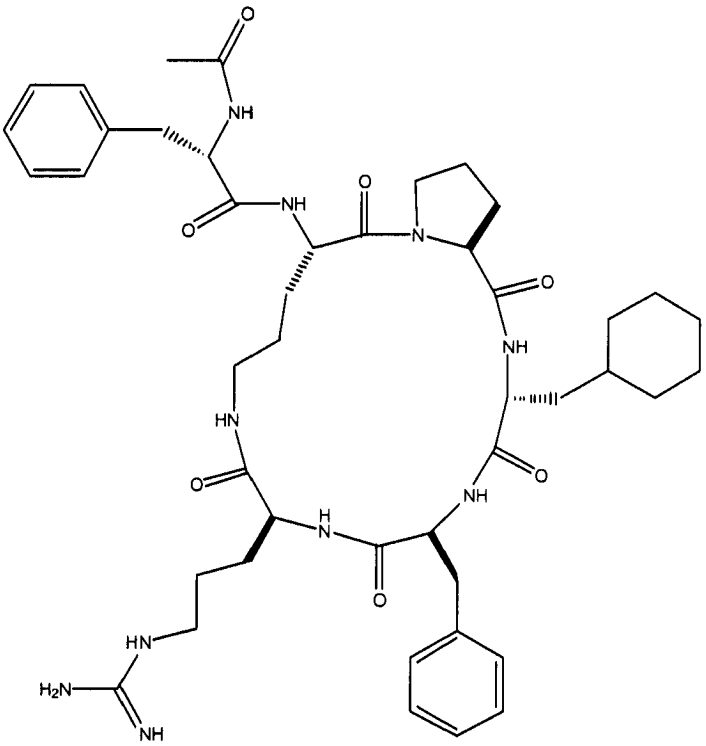

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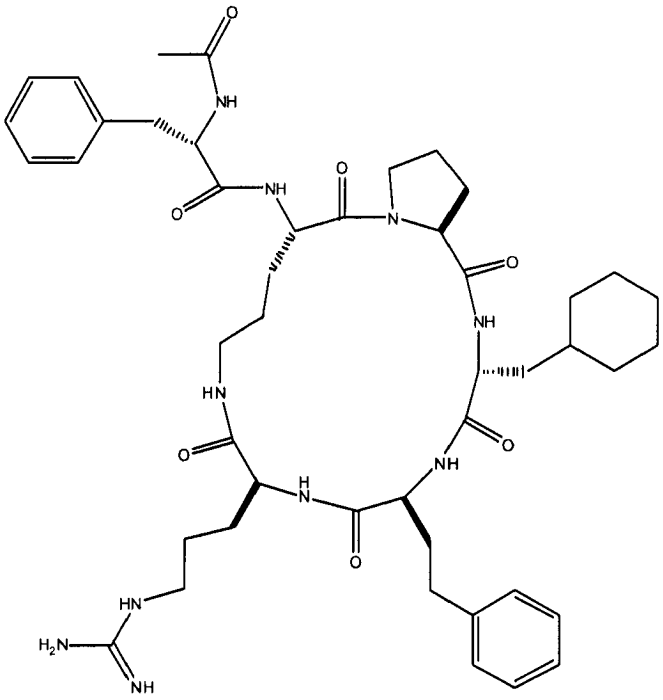

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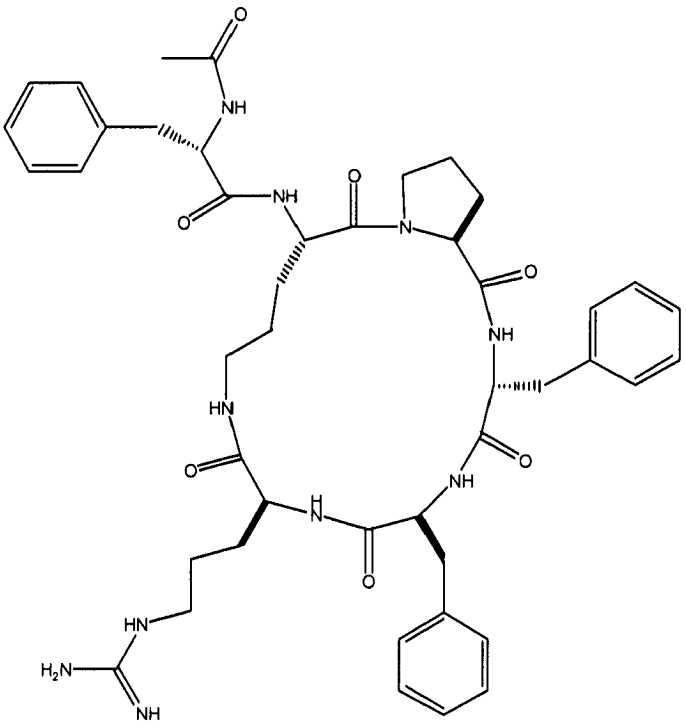

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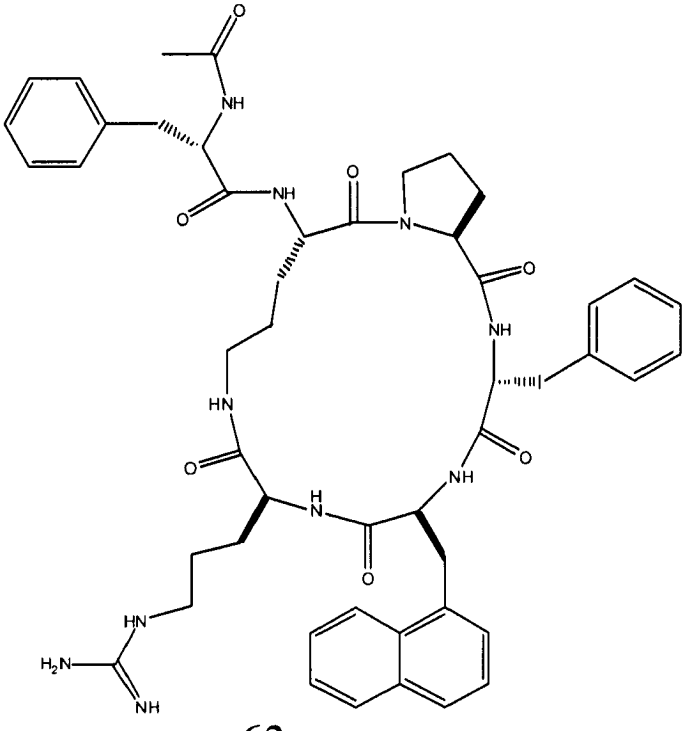

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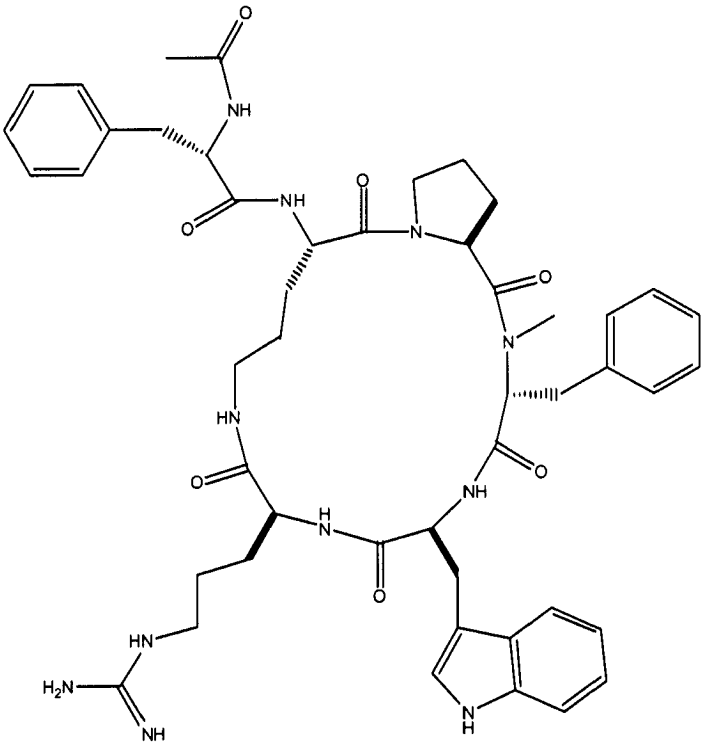
and



64

In a particularly preferred embodiment, the compound is PMX53 (compound **1**), compound **33**, compound **60** or compound **45** ~~described therein~~illustrated *supra.*

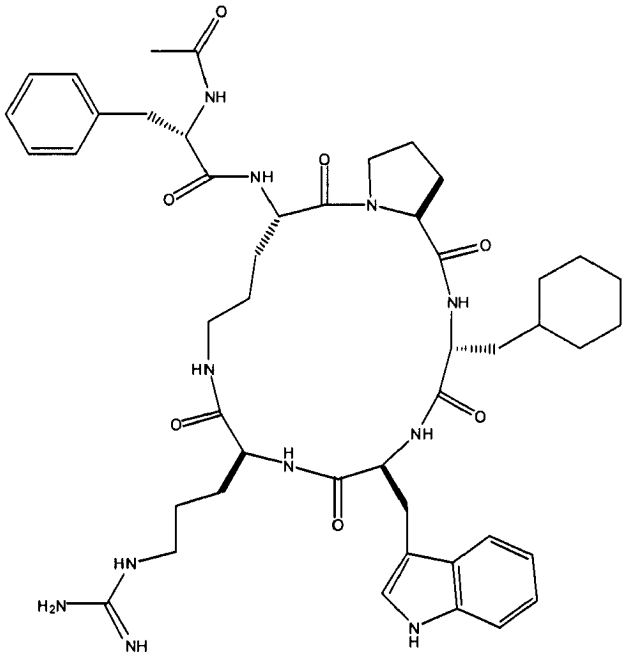
Please replace the paragraph appearing in the substitute specification filed on 4/14/05 at page 8, lines 25-29, with the following amended paragraph, which supersedes the intervening amendments filed on 6/29/06 and 10/16/07:

An "uncommon" amino acid includes, but is not restricted to, D-amino acids, homo-amino acids, N-alkyl amino acids, dehydroamino acids, aromatic amino acids other than phenylalanine, tyrosine and tryptophan, ortho-, meta- or para-aminobenzoic acid, ornithine,

citrulline, canavanine, norleucine, ~~□-glutamic~~ γ-glutamic acid, aminobutyric acid, L-fluorenylalanine, L-3-benzothienylalanine, and α,α-disubstituted amino acids.

Please replace the paragraph appearing in the substitute specification filed on 4/14/05 at page 12, lines 4-10, with the following amended paragraph, which supersedes the intervening amendments filed on 6/29/06 and 10/16/07:

Compounds **1-6, 17, 20, 28, 30, 31, 36 and 44**, shown above (and also disclosed in International [[p]]Patent [[a]]Application ~~No.PCT/AU98/00490~~ No. PCT/AU98/00490) and compounds **10-12, 14, 15, 25, 33, 35, 40, 45, 48, 52, 58, 60, 66, and 68-70**, also shown above and disclosed for the first time in Australian ~~provisional application~~ PCT International Patent Application No. PCT/AU02/01427 have appreciable antagonist potency (~~IC50~~IC_{50} < 1 μM) against the C5a receptor on human neutrophils. The compounds shown below, PMX53 (compound **17**), [also disclosed in International Patent Application No. ~~of~~ PCT/AU98/00490 ~~also identified~~ and identified as compound **1** in International Patent Application No. PCT/AU02/01427] ~~PCT/AU02/01427)~~ and compounds **33, 45** and **60** herein [also disclosed in International Patent Application No. PCT/AU02/01427] ~~of PCT/AU02/01427~~ are most preferred:



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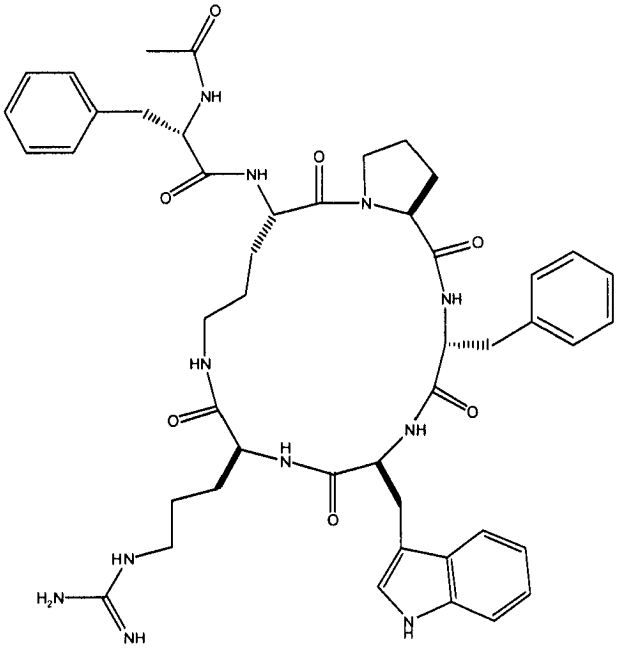

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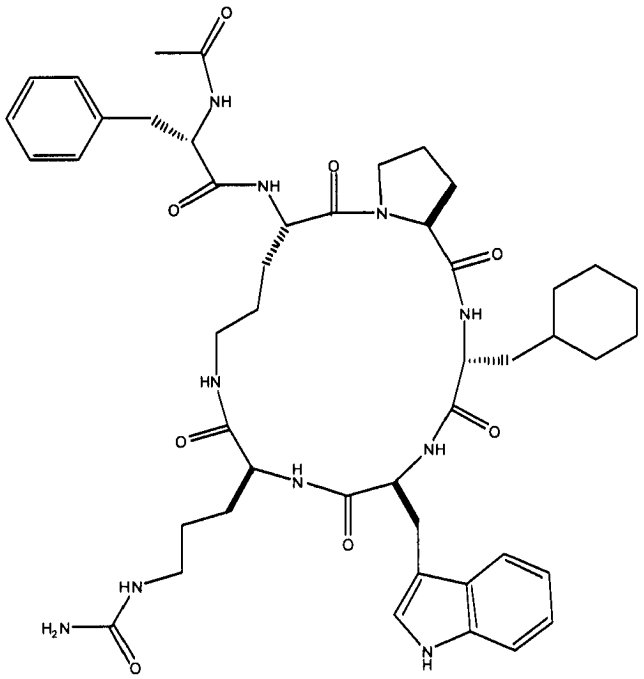

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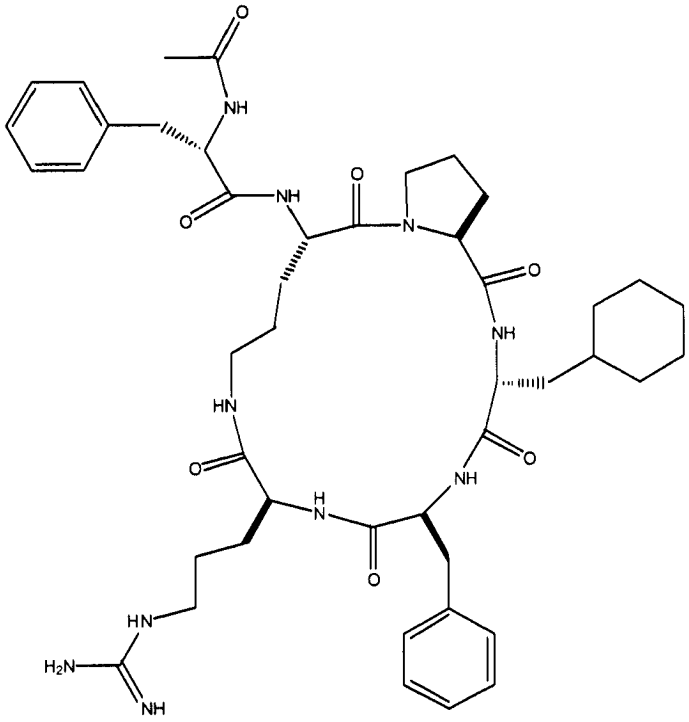

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Please replace the paragraph appearing in the substitute specification filed on 4/14/05 at page 12, lines 19-28, with the following amended paragraph, which supersedes the intervening amendments filed on 6/29/06 and 10/16/07:

Assays are performed with fresh human PMNs, isolated as previously described (~~Sanderson *et al*, 1995~~ Sanderson *et al.*, 1995) using a buffer of 50 mM HEPES, 1 mM $CaCl_2$, 5 mM $MgCl_2$, 0.5% bovine serum albumin, 0.1% bacitracin and 100 μM phenylmethylsulfonyl fluoride (PMSF). In assays performed at 4~~□C~~4°C, buffer, unlabelled human recombinant C5a (Sigma) or peptide, Hunter/Bolton labelled ^{125}I-C5a (~ 20 pM) (New England Nuclear, MA) and PMNs (0.2×10^6) are added sequentially to a Millipore Multiscreen assay plate (HV 0.45) having a final volume of 200 μL/well. After incubation for 60 min at 4~~□C~~4°C, the samples are filtered and the plate washed once with buffer. Filters are dried, punched and counted in an LKB gamma counter. Non-specific binding is assessed by the inclusion of 1 mM peptide or 100 nM C5a, which typically results in 10-15% total binding.

Please replace the paragraph appearing in the substitute specification filed on 4/14/05 bridging page 12, line 33 to page 13, line 8, with the following amended paragraph, which supersedes the intervening amendments filed on 6/29/06 and 10/16/07:

Cells are isolated as previously described (Sanderson *et al*, 1995) and incubated with cytochalasin B (5μg/mL, 15 min, ~~37□C~~37°C). Hank's Balanced Salt solution containing 0.15%

gelatin and peptide is added on to a 96 well plate (total volume 100 µL/well), followed by 25 µL cells (~~4x106/mL~~4 × 10^6/mL). To assess the capacity of each peptide to ~~antagonise~~antagonize C5a, cells are incubated for 5 min at ~~37□C~~37°C with each peptide, followed by addition of C5a (100 nM) and further incubation for 5 min. Then 50 µL of sodium phosphate (0.1M, pH 6.8) is added to each well, the plate was cooled to room temperature, and 25 µL of a fresh mixture of equal volumes of dimethoxybenzidine (5.7 mg/mL) and H_2O_2 (0.51%) is added to each well. The reaction is stopped at 10 min by addition of 2% sodium azide. Absorbances are measured at 450 nm in a Bioscan 450 plate reader, corrected for control values (no peptide), and analysed by non-linear regression.

Please replace the paragraph appearing in the substitute specification filed on 4/14/05 at page 21, lines 9-18, with the following amended paragraph, which supersedes the intervening amendments filed on 6/29/06 and 10/16/07:

Example 7 Postoperative anti-inflammatory treatment

In the experiments involving the surgical severing of the cruciate ligament in dogs, ~~desribed~~ described in Example 3, it was noted that dogs treated with PMX53 recovered from surgery more rapidly than placebo-treated dogs. Dogs undergoing routine orthopaedic surgery, for example for repair of ruptured cruciate ligaments, repair of luxated patella and removal of damaged menisci, are frequently given NSAIDs postoperatively to reduce inflammation and reduce pain. A blinded study with PMX53 and a NSAID such as meloxicam is performed to test whether PMX53 is effective in managing postoperative pain and in

improving outcomes after surgery. This trial is performed in a specialist orthopaedic veterinary practice in order to have access to suitable dogs which are undergoing routine surgery.

Please replace the paragraph appearing in the substitute specification filed on 4/14/05 at page 21, lines 21-33, with the following amended paragraph, which supersedes the intervening amendments filed on 6/29/06 and 10/16/07:

Cyclic peptides have several important advantages over acyclic peptides as drug candidates (~~Fairlie et al 1995, Fairlie et al, 1998,~~ Fairlie *et al.*, 1995, Fairlie *et al.*, 1998, Tyndall and Fairlie, 2001). The cyclic compounds described in this specification are stable to proteolytic degradation for at least several hours at ~~37□C~~37°C in human blood or plasma, in human or rat gastric juices, or in the presence of digestive enzymes such as pepsin, trypsin and chymotrypsin. In contrast, short linear peptides composed of L-amino acids are rapidly degraded to their component amino acids within a few minutes under these conditions. A second advantage lies in the constrained single conformations adopted by the cyclic and non-peptidic molecules, in contrast to acyclic or linear peptides, which are flexible enough to adopt multiple structures in solution other than the one required for receptor-binding. Thirdly, cyclic compounds such as those described in this invention are usually more lipid-soluble and more pharmacologically bioavailable as drugs than acyclic peptides, which can rarely be administered orally. Fourthly, the plasma half-lives of cyclic molecules are usually longer than those of peptides.